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SYPHILIS OF THE NERVOUS SYSTEM AND ITS TREATMENT.¹

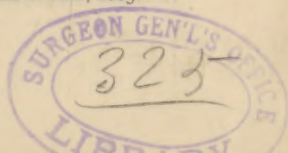
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THE task which lies before me to-night is no easy one. It is the task of explaining, within a short space of time, the symptoms that may arise from a disease which affects the whole of the complicated machinery of the brain, the spinal cord, and the peripheral nerves. I cannot hope to do more than outline the subject. To treat it exhaustively would require a book, to which this paper might serve as an introduction.

Some idea of medical interest in the matter may be obtained from a somewhat curious comparison. Professor Max Müller, the well-known philologist, informs us that the whole of the Sanscrit literature, running, as he expresses it, "like a high mountain-path of literature through the whole history of India, and extending over a period of three or four thousand years, is contained in about 10,000 manuscripts"—more, the same authority estimates, than the whole classical literature of Greece and Italy put together.² I have been able to count up some 500

¹ Read, by invitation, before the Philadelphia Neurological Society, April 25, 1887.

² India: What can it Teach us? By F. Max Müller, 1883.



different articles that have been written on the subject of syphilis in the last thirty years, and there are probably many more. This is one-twentieth of the whole Sanscrit literature, or of the combined classical literature of Italy and Greece; and, therefore, in order that the literature of this one subject should equal these great national literatures, it would only take the time of about 600 years, or one-seventh to one-fifth of the time of the Sanscrit writings.

Syphilis of the nervous system varies essentially from the syphilis about which the great syphilographers of France, England, and America have written so voluminously, because the phenomena of the disease which they described have been almost entirely confined to the cutaneous surface of the body. When this malady, however, affects the nervous centres and their peripheral appendages, it usually, I am prepared to say, has not been marked in its cutaneous manifestations. Most of the cases I have had the fortune to see had this peculiarity. At the outset, therefore, we are met with one great difficulty, which does not bar the way of the dermatologist—we are deprived of the diagnostic guidance of a group of symptoms which have been carefully studied for many years; and in their place no one has as yet suggested an equally pathognomonic group of nervous symptoms. Unguided by the tell-tale signs upon the exterior of the body, the history of the initial lesion may, as is probably well known to most of you, become very obscure. The primary sore being usually very slight, it may very easily be overlooked, even by those who are in search of it. The infection may come through the husband to the wife, innocently, too, so far as the latter is concerned. Not long ago I heard a lady telling some friends how she had been afflicted with an obstinate

headache and subsequent inflammation of the eyes. Now, it so happened that this lady's husband had died a short while before of intracranial syphilis, and on going to her attending physician, I found that he was entirely ignorant of the etiology of his patient's symptoms. The infection may also come through a surgical operation, as is probably known to you; for I suppose that there are very few communities of any size in which physicians cannot be found who have infected themselves in this manner. Or the infection may come through a lesion innocently acquired about the buccal cavity, and even, perhaps, through articles of clothing. Infection through heredity is of no small account. For these different reasons, it may readily occur that many individuals may be entirely unaware of the disease of which they are the bearers. Add to these sources of error the tendency to concealment which so often actuates patients, glandular indurations, exostosis, in hereditary syphilis the peculiar teeth described by Hutchinson, and the record of many miscarriages and dead births. All these latter incidents may greatly assist us when they are present, which, unfortunately, they are not in a number of cases of nervous syphilis.

At the outset, it should be clearly understood that syphilis may affect the whole of the nervous system—the brain, spinal cord, peripheral nerves, membranes, sheaths, and the bony structures surrounding the nervous tissues, and the bloodvessels within the nervous tissues. It may assume the form of a diffuse infiltration, or it may be limited to a gumma, or it may be confined to the arteries, or there may be diffuse infiltrations, gummata, and arterial lesions in one subject. This diffuse infiltration takes its departure from the capillaries, and consists of numbers of round cells spread throughout surrounding

tissues. These are the round cells of the shape of those formations to which Virchow has given the name of granulation tumors, and for which other German pathologists have suggested the name of infectious-granulation-tumors, to which class belong the tubercular formations, lupus, lepra, actinomycosis, and glanders. The cellular character and behavior of each one of these different species are, as is well known, different, as is also their particular location within the body; and two of the salient characteristics of the cells thrown out in a syphilitic infiltration are: that they have scarcely any tendency to suppuration, undergoing a retrogressive metamorphosis by non-suppurative transformations, and that the individual cells are endowed with extraordinarily long-lived vitality. These cells may often lie among the normal tissues for long periods of time and not do any really structural damage. On the other hand, they may set up truly destructive processes that may injure the component parts of a tissue as much as any other destructive process whatsoever.

The arterial lesions were first described in 1874, by Dr. Heubner, of Leipsic, whose observations have given rise to further and often contradictory investigations by Köster, Friedländer, Baumgarten, Rumpf, and many others. Heubner advanced the view that in syphilitic vessels the endarteritis was peculiar in its place of origin, which was in the vessel-less tissue that lies between the *membrana fenestrata* and the endothelium. Normally the *membrana fenestrata* and the endothelium lie so close to one another that no intervening tissue can be seen microscopically. In syphilitic endarteritis, however, Heubner maintains, they are widely separated by a new cellular formation, which consists of a proliferation of endothelial cells, to which, after a cer-

tain time, there are added numbers of round cells, as in the ordinary granulation tumors. Heubner very minutely and carefully describes the differences in size of the endothelial cells in health and disease, as well as how to obtain an endothelium that has not been bruised by the ordinary act of cutting the vessel, and it is difficult for any one who reads his painstaking brochure to refuse credence to his plea for this peculiar anatomical site of syphilitic endarteritis, nor is it easy to resist the wish that it were true, as it would constitute so invaluable a guide in dubious cases. But in the thirteen years that have elapsed since Heubner first made his views public, no one has fully confirmed him. Köster, Friedländer, Baumgarten, Huber, Schottelius, Marchand, Rumpf, deny that the endarteritic process starts in the vessel-less structure between the *membrana fenestrata* and the endothelium, or that it consists at first of an endothelial proliferation. They maintain, on the contrary, that the endarteritis is due to the outpouring of round cells from the minute nutritive vessels of the vessels themselves—from the *vasa vasorum*—contained in the outer coats, and that the endothelial proliferation is only a part of the general cellular disturbance that takes place in consequence of this outpouring of round cells. The question needs further investigation. But, however it may be decided, there is no diversity of opinion as to the results which follow upon the endarteritis. The vessels may become narrowed in their lumen by the thickening inward of the fenestrated membrane and the intima. They may become entirely occluded from the same cause. The inner surface of the intima may become roughened or altered in its chemical constitution, and a thrombus may form, which may, in its turn, give rise to an

embolus. It may even happen, rarely however, that minute aneurisms may be formed from the wasting of the muscular coat of the vessel, and occasionally there may be a hemorrhage. In other words, a syphilitic infiltration may set up an endarteritis which usually leads to a narrowing of the canal of the vessels, or to an occlusion of it, but which may occasionally lead to thrombi, emboli, aneurism, and hemorrhages.

The prevailing tendency of thought among modern pathologists has naturally led to an endeavor to trace syphilis to a microörganism. As is usual in researches of this kind, our German friends have led the van. As far back as 1869 Hallier thought that he had detected peculiar microbes in the blood corpuscles, and Lustdorfer described syphilitic bodies in the blood. These statements do not seem, however, to have been verified. Klebs, in 1879, Aufrecht, in 1881, and Birch-Hirschfeld, in 1882, described microörganisms which they would have us regard as the cause of the phenomena of syphilis. But the investigations of Lustgarten and Doutrelepoint since 1884 have been more precise than those of their predecessors, have been largely confirmed, and have, therefore, attracted far more attention. These gentlemen have described slender bacilli, like straight or somewhat curved rods of about the size of the tubercular bacilli, and they are found singly or in groups in cells. They bear spores, which appear as clear, oval, glittering spots. They are colorable by a method described by Lustgarten. A most energetic discussion of these bacilli, their relations to syphilis and their differentiation from other bacilli, has been and is still going on in France and Germany. The mere catalogue of the disputants will indicate the interest that is felt in the

subject—Cornil, Giacomini, Disse and Taguchi (two Japanese medical men writing in German), Klemperer, Köbner, Matterstock, Rumpf, Gottstein, Leloir, Weigert, Baumgarten, Tavel, Alvarez, Eve, Longuard. As a result, it may be stated, that the question is not by any manner of means yet decided; that the bacilli described by Lustgarten have been found by many in syphilitic individuals; that bacilli, similar in some respects to those of Lustgarten, are found in normal smegma and the secretions of the genital organs; that the bacilli of Lustgarten and those of the smegma and the genital secretions differ from one another distinctly in several particulars; that there are probably several bacilli in syphilis, two varieties being described by Rumpf. The bacilli of Lustgarten have been found in all stages of syphilis and in syphilitic alterations in many different tissues, and nothing like them has been found in non-syphilitic individuals, except in the smegma or the genital secretions, and even here there are alleged points of difference: hence it would certainly seem as if Lustgarten's bacilli bore some relation to syphilis. No one has as yet succeeded in obtaining any pure cultures of these bacilli, and this test is therefore lacking.

So much do we know of the pathology of syphilis.

These diffuse infiltrations, these gummata, these arterial lesions, may, as must be evident to all of you, cause symptoms that are coextensive with the symptoms of derangement of any part of the nervous system. All the recognized mental and nervous disorders may have a syphilitic basis, and in the case of any one of them it simply becomes a question as to whether a history of the infection is obtainable. So far as is known, it is not possible to say of any nervous or mental disorder that it may not have a

syphilitic causation; and if we may draw conclusions from the nervous and mental disorders of recognized syphilitic causation, we should say that the prognosis of very few would be materially altered by such etiology. But over and above the well-recognized forms of nervous and mental disease, there are certain groups of symptoms which may fairly be regarded as indicative of specific infection, although the proof may not be greater than that to which the lawyers give the name of "prima facie"—*i. e.*, proof amounting to a presumption, which may, however, be rebutted by adequate testimony to the contrary. These symptom-groups, if I may allowed to formulate from my own experience, are as follows:

1. Quasi-periodical cephalalgia of a peculiar kind.
 2. Hemiplegia under forty years of age, with or without preceding cephalalgia of the aforesaid type.
 3. Cephalalgia followed by hemiplegia, which bear a singular relationship to one another in that the cephalalgia ceases immediately upon the super-vention of the hemiplegia, and does not recur.
 4. Convulsions in the adult, which have not been preceded by convulsions in infancy, and are not of traumatic or nephritic origin, or due to pregnancy, or in an individual subject to migraine.
 5. Symptoms indicative of a lesion at the base of the brain.
 6. A comatose condition extending over days or weeks, not traumatic, meningitic, diabetic, nephritic, or from typhoid fever.
 7. Tabes dorsalis.
 8. General paresis.
 9. Spinal lesions in a subject who has had intra-cranial syphilis.
 1. *Quasi-periodical cephalalgia of a peculiar kind.*
- One expression of the quasi-periodicity of syphi-

litic cephalalgia that is well known to the profession is the nocturnal recurrence. But this characteristic may be other than nightly. I have known the headache to recur repeatedly at a certain time of the day, usually in the afternoon. What is very misleading, too, in the way of differentiation of malaria is that this cephalalgia may yield readily, although temporarily, to large doses of quinine. This quasi-periodical form of neuralgia may be accompanied by an obstinate insomnia, and by considerable mental irritability, both insomnia and irritability bearing no adequate proportion to the amount of pain; when the latter signs are present, they are of considerable diagnostic importance, because the cephalalgia of brain tumor or nephritis is not usually accompanied by them.

2. *Hemiplegia under forty years of age, with or without preceding cephalalgia of the aforesaid type.* It is a fair clinical distinction that can be used for guidance of one's inquiry, upon first talking with a patient, to bear in mind that hemiplegia in the adult under forty years of age is usually of syphilitic origin, whilst hemiplegia in the adult above forty years of age is due to the chronic degenerative endarteritis of middle life and old age. Hemiplegia may occur in children, of course, from many other causes, and should, therefore, be ruled out in the present inquiry. This adult hemiplegia of specific origin may be either motor or sensory, or both, for anatomical reasons that need not be explained.

3. *Cephalalgia followed by hemiplegia, which bear a singular relationship to one another, in that the cephalalgia ceases immediately upon the supervention of the hemiplegia, and does not recur.* This is a curious clinical feature to which, so far as I know, no writer has yet made allusion, and one which I

have observed in over forty cases, although I can offer no explanation of it whatsoever. I have never seen it except in syphilitic hemiplegia. I should like to ask the attention of the profession to this point, in order that it may be tested.

4. *Convulsions in the adult, which have not been preceded by convulsions in infancy, and are not of traumatic or nephritic origin, or due to pregnancy, or in an individual subject to migraine.* It is too much the custom, I think, to regard convulsions in infancy as harmless, and not prone to recurrence. In a paper which I read several years ago,¹ I called attention to the fact that a large proportion of the cases of epilepsy in youths or adults, would be found upon careful inquiry to have had a convulsion in early life, that had usually been attributed to dentition or intestinal or febrile complaints; and of such early convulsions it may be very difficult to obtain a history unless the parents or some other near relatives are interrogated. The convulsions occurring in nephritis, or in certain women during pregnancy, are too well known to need more than a bare reference. Again, it is a curious fact, to which I have referred in the paper just mentioned, that migraine is interconvertible in certain individuals with epilepsy, so that most individuals who have a personal or hereditary history of migraine will be found upon minute and patient interrogation to have had a loss of consciousness or epileptic-like convulsion at some period of their life. If, however, pregnancy, migraine, nephritis, trauma, and preceding infantile convulsions, are excluded,

¹ The Treatment of Epilepsy, N. Y. Med. Journal, June 28 and July 5, 1884.

a convulsion in an adult should give rise to grave suspicions of intracranial syphilis.

5. *Symptoms indicative of a lesion at the base of the brain.* Syphilis is especially apt to hug the base of the brain, and more especially that anterior portion of it which forms the hexagon wherein lie the olfactory, the optic, the motor oculi, and the fourth pair of nerves, as well as the crura cerebri, and lesions of which impair the functions of these cranial nerves on one side of the body, and induce disturbances of motion and sensation upon the opposite side, giving rise to the so-called "crossed paralysis." Of course, tuberculosis has a predilection for the same site, but the history of the patient and the presence of pulmonary symptoms make easy a diagnosis of this affection. It is true also that tumors of non-specific origin may be found in the same location, but usually they are not so diffuse as a syphilitic infiltration, and usually also the specific lesions of this part of the brain are accompanied or have been preceded by a characteristic cephalalgia.

6. *A comatose condition extending over days or weeks, not traumatic, meningitic, diabetic, nephritic, or from typhoid fever.* It is not always easy to exclude the coma of meningitis, especially in the early stage before the characteristic symptom of retraction of the head has made its appearance, although the temperature curve may be of great assistance. In my experience, this retraction of the head is of well-nigh infallible importance. Fränkel, however, has reported a rare and curious case, from the wards of the Charité Hospital in Berlin, in which this retraction of the head was found (post-mortem) to be due to a lesion in the middle portion of the ascending frontal convolution, just where the centre for the muscles of the neck has been located on *à priori* grounds by Wer-

nicke. The coma of nephritis, it must also be borne in mind, is not always of the profound nature that is seen where the urine contains large amounts of albumen. It may be light, variable in its manifestations, simulating a profound hysterical condition. Nor will it do to exclude nephritis by a mere cursory examination of one specimen of the urine for albumen. Several specimens should be obtained. Best one at morn, midday, and evening, and the amount of urea should be estimated, casts, blood-corpuscles, and pus should be carefully searched for, and albumen should be sought for by the finer modern methods, rather than by the old and rough test by heat and nitric acid. I have more than once been called into consultation regarding conditions of coma, and have been informed that nothing had been found in the urine to indicate nephritis, and yet the autopsy has disclosed advanced disease of the kidney. Diabetes can, of course, be easily ascertained. Some anomalous cases of typhoid fever are apt to mislead one at the start, although the progress of the disease almost invariably makes the diagnosis very certain.

7. *Tabes dorsalis*, and

8. *General paresis*.

It is not of much practical importance to ascertain the presence or not of a specific infection in these two grave maladies, because, so far as I have seen, the syphilitic causation has for them only this significance, that they will do rather better upon anti-specific treatment than the non-syphilitic cases; the course of the disease, however, is not materially altered.

9. *Spinal lesions in a subject who has had intracranial syphilis*. These spinal infections always re-

quire unusually large doses of the anti-specific remedy.

This quasi-periodical cephalalgia, this hemiplegia under forty years of age, this cephalalgia ceasing upon the supervention of hemiplegia, these convulsions in the adult, these lesions at the base of the brain, these comatose conditions may be present singly or in varied grouping, and singly or in groups they should always give rise to a strong suspicion of antecedent specific infection.

We have seen how difficult it may be to obtain the precise history of the initial lesion in such cases. The question at once arises as to what significance may attach to the success or non-success of anti-specific treatment. There can be no question that the profession are illogical in attaching the importance that they usually do to the results of such anti-specific treatment, because mercury and the iodides are efficacious in many affections that have no specific etiology. All the same, however, I cannot disabuse my mind of the fast-rooted impression that a disease which disappears rapidly and completely under anti-specific treatment, and which has not been affected by other forms of medication, is of specific origin.

The *prognosis* is dependent upon the question as to whether the lesions are destructive or non-destructive, and in many cases it is treatment alone that can determine this point. In general terms it may be said that syphilis of the nervous system is of good prognosis except where it has set up actual organic disease, except where it has excited in the normal tissue the formation of some other structure that is foreign to the particular texture. The infiltrations of the nervous tissues themselves, the gummata, the arterial lesions, are by themselves remarkably harm-

less. It is singular to see, as we often do, how much and how long the nervous structure will present evidences of syphilitic disease and yet recover entirely under adroit and vigorous treatment. Buzzard tells of an artery that had been almost occluded, being tested by the sphygmograph and yet was freed by proper treatment. To speak more precisely, it may be said that the symptoms of good omen are:

Nervous syphilis in its early stage; lesions at the base of the brain; spinal lesions without preceding intracranial specific disease; peripheral lesions.

Of uncertain omen are:

Long standing nervous syphilis;

Syphilitic insanities;

Spinal lesions with preceding intracranial specific disease;

Convulsions;

Comatose conditions;

Hemiplegia.

Of bad omen are:

Tabes dorsalis;

General paresis;

Nervous syphilis in persons whose general health is bad;

Relapses in spite of anti-specific treatment;

Nervous syphilis in persons who bear the iodides badly.

I have very pronounced ideas in regard to *treatment*. I know of no reason for dogmatism except considerable experience, and that is my excuse for my dogmatism. I have no faith whatsoever in mercury, and I have discontinued its use for some time past. Again and again have I seen cases go halting along in the most uncertain manner, under mercurial treatment, and yet have the symptoms been smoothly, gradually, and certainly removed by the iodides.

In several cases, too, I have known of death, although the most careful mercurial treatment had been pursued in enormous doses, and these cases have been precisely similar, as far as anyone is able to judge of one case by another in the practice of medicine, to others that I have been accustomed to regard as of favorable prognosis under the treatment by the iodides. I am quite prepared to say, that unless the iodides with their proper adjuvants—of which I shall speak in a moment—can cure a case of nervous syphilis, it cannot be cured at all. But the dose of the iodides which are administered by the Germans and French will often be entirely inadequate. I give the iodides until the symptoms yield, or until iodism is produced. I make use of the saturated solution of the iodide of potash, each drop of which contains almost a grain of the salt. I commence with twenty drops three times a day, and increase it each day by two or three drops at each dose, and keep increasing until the symptoms yield or iodism is produced. Should iodism ensue before the symptoms yield, I pursue one of two methods. I first increase the dose of the iodide by about one-third, and rapidly increase each succeeding day. Singular to say, in some cases this increased dosage will cause the iodism to disappear, and the larger doses will be borne very well. Should, however, these larger doses still more increase the iodism, I decrease to one-half of the dose at which the iodism had begun, and continue this decreased dose until the iodism diminishes or disappears, when I again rapidly increase the dose, and am usually able to go on without further trouble. In some few individuals, however, no amount of care will cause more than a certain amount of the iodide to be borne, and such cases, as I have said, are usually of unfavorable prognosis.

In some cases, too—fortunately they are rare—even small doses of the iodide will produce a cardiac disturbance that prohibits its administration. But this last fact should not be confounded with the phenomenon that the profession generally does not seem to be cognizant of, namely, that small doses of the iodide, five or ten grains, will usually produce more iodism than the larger doses. I am perfectly well aware that the medical chemist will object that these large doses of the iodide pass through the body and are quickly excreted by the urine; but I am equally well aware, in the face of this fact, that these large doses of the iodide will cause symptoms to yield that cannot be made to yield by lesser doses. I have given as much as eight hundred grains of the iodide of potash in the twenty-four hours, and have seen symptoms disappear with these enormous doses that would not yield to minor ones. I administer the iodide after meals, and either in a full tumbler of ice-water, or in a glass of Vichy, or in a glass of a Bohemian spring water, the Giesshübler. I prefer the Giesshübler to the Vichy, although it is more expensive, because it is much more pleasant to the taste, and agrees much better with the average stomach. Moreover, the Vichy water which is put up in siphons in this country is artificial, by no means equal in its effects to the natural water, and the natural water, either of this country or of Europe, does not keep as well in bottles as does the somewhat similar water of the Bohemian spring.

But he who expects to cure his patient with the iodides alone, unless the case be so grave as to call for immediate relief, will be disappointed. The human organism must be put in the best possible condition. A generous diet should be employed. Freedom

from care and worry, where possible, should be enjoined, and all strenuous exertion of body or mind avoided. And let me say here that in many broken-down individuals the most satisfactory results may be obtained from a conjunction of the iodides with the brilliant treatment that has been made known by Dr. Weir Mitchell, under the name of "Fat and Blood making"—a therapeutical procedure that, in my humble opinion, will rank in coming years with the surgical revolution inaugurated by Lister. When the acute symptoms have been brought under control, travel, especially an ocean voyage, will often work wonders. In every case that tends to chronicity staple tonics and alteratives should be used.

I have often asked myself, when a person can be considered to be cured of nervous syphilis; and I have never succeeded in answering the question to my own satisfaction. I know of no data by which we can guide ourselves. I have seen relapses occur years after the disappearance of every untoward symptom, and I have seen them even where a certain moderate treatment by the iodides had been maintained. I usually impress this uncertainty upon my patients, warn them to be on the lookout for future symptoms, and apprise whoever may be their attending physician of their possible significance, and I enjoin them to keep up moderate doses of the iodide for years. This last precaution I observe the more readily because I have but seldom seen any ill-effects from the continued administration of the iodides, to which patients usually become accustomed as they do to common salt. Occasionally it may happen that an obstinate pharyngeal or post-nasal trouble may be induced, or some unsightly cutaneous eruption, but, as a rule, these are controllable,

and in any event they are far preferable to the possibilities of nervous syphilis.

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